Gene test information

ALPHA-1-ANTITRYPSIN (AAT) DEFICIENCY (SERPINA1 MUTATIONS)

- **Background**

  The protease inhibitor alpha-1-antitrypsin (AAT), found in high concentrations in the plasma, inhibits trypsin and also neutrophil elastase. AAT deficiency leads to an unchecked action of trypsin and elastase. Pulmonary emphysema, chronic obstructive pulmonary disease etc. are among the most common symptoms caused by an AAT deficiency. Furthermore, due to the toxic effect of the accumulated AAT on the liver cells, clinical pictures such as cirrhosis of the liver and even liver carcinoma are among other late sequelae.

- **Causes of AAT deficiency**

  The causes of AAT deficiency are mainly two variants of SERPINA1 gene, which encodes AAT. In contrast to normal alleles (M), the risk alleles Z and S are associated with considerably lower plasma concentrations of AAT. The Z variant is by far the most common and diagnostically significant deficient allele (in 95% of all patients with severe AAT deficiency) whereas heterozygous (MZ or SZ) and homozygous SS carriers as a rule only fall ill if there are additional risk factors involved such as smoking. With early diagnosis, patients can accordingly avoid negative factors, clinical late sequelae can be prevented or minimised. With an incidence of 1:2.000, AAT deficiency is one of the most common potentially lethal hereditary diseases in Europe.

- **SERPINA1 genotypes**

Genotype	Commentary
MM, MS, SS	No Z-allele present. AAT levels normal or only modestly reduced.
MZ, SZ	Heterozygous carrier of a Z-allele. AAT-levels decreased by about 50% (MZ) to 70% (SZ). Modestly increased risk for AAT deficiency-related diseases of lung or liver.
ZZ	Homozygous carrier of a Z-allele. AAT-levels strongly reduced. Without treatment, about 75% of carriers of this genotype will develop AAT deficiency-related diseases of lung or liver.

References:

Luisetti, Epidemiology of alpha1-antitrypsin deficiency. Thorax 2004;59:164-9.

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